Application No.: Filing Date:

09/646,950

December 8, 2000

AMENDMENTS TO THE CLAIMS

1-14. (Canceled)

15. (Currently amended) The method of Claim 71A method of reducing the processing of a protein antigen by a MHC Class II molecule by a cell, the method comprising contacting the cell with an inhibitor of asparaginyl endopeptidase, wherein

the inhibitor of asparaginyl endopeptidase is a competitive inhibitor comprising a peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) (SEQ ID NO: 1) and Lys-Asn-Asn-Glu-NH (KNNE) (SEQ ID NO: 2); or

the inhibitor of asparaginyl endopeptidase is a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith.

- 16. (Original) A method according to Claim 15 wherein the inhibitor is a competitive inhibitor.
- 17. (Canceled)
- 18. (Previously presented) A method according to Claim 16 wherein the peptide is N and C-terminal blocked.
- 19. (**Previously presented**) A method according to Claim 15 wherein the inhibitor is a non-competitive inhibitor.
- 20. (**Previously presented**) A method according to Claim 19 wherein the inhibitor has the structure B1-(X)_n-Asn-Q where B1 is any suitable N terminal blocking group; X is an amino acid residue; n is between 1 and 100, Asn is an asparagine residue and Q is a group capable of reacting with the active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith.

21-37. (Canceled)

38. (**Previously presented**) A pharmaceutical composition comprising a competitive inhibitor of asparaginyl endopeptidase and a pharmaceutically acceptable carrier,

wherein the competitive inhibitor of asparaginyl endopeptidase comprises an N and C-terminal blocked peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) (SEQ ID NO: 1) and Lys-Asn-Asn-Glu-NH (KNNE) (SEQ ID NO: 2).

39. (Canceled)

Application No.: 09/646,950

Filing Date: December 8, 2000

40. (Canceled)

A pharmaceutical composition according to Claim 38 further 41. (Original) comprising an immunosuppressive agent.

42. (Previously presented) A pharmaceutical composition comprising the composition of Claim 52 and a pharmaceutically acceptable carrier.

43-51. (Cancelled)

- 52. (Previously presented) An inhibitor of asparaginyl endopeptidase which has the structure Bl-(X_aX_n)Asn-Q wherein B1 is any suitable N terminal blocking group; X_aX_n are the n amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules; Asn is an asparagine residue; and Q is a group capable of reacting with the active site of asparaginyl endopeptidase and forming a covalent complex therewith.
- 53. (Previously presented) An inhibitor according to Claim 52 wherein the number of amino acid residues in (X_aX_n) is between 1 and 25.
- 54. (Original) An inhibitor according to Claim 53 which is any of Bl-Ser-Gln-Asn-Q; Bl-Leu-Glu-Asn-Q; Bl-Leu-Gln-Asn-Q; Bl-Pro-Glu-Asn-Q; Bl-Leu-Lys-Asn-Q; Bl-Gln-Asn-Q; B1-Glu-Asn-Q; B1-Asp-Glu-Asn-Q; B1-Asn-Gly-Asn-Q; B1-Phe-Pro-Asn-Q; B1-Val-Pro-Asn-Q; and Bl-His-His-Asn-Q.

55. (Canceled)

56. (Previously presented) A composition comprising an inhibitor of asparaginyl endopeptidase and an inhibitor of cathepsin S, wherein

the inhibitor of asparaginyl endopeptidase is a competitive inhibitor comprising peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) (SEQ ID NO: 1) and Lys-Asn-Asn-Glu-NH (KNNE) (SEQ ID NO: 2); or

the inhibitor of asparaginyl endopeptidase is a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith.

57-59. (Canceled)

60. (Currently amended) A method according to Claim 15 wherein the antigen presenting cell is, or is comprised in a tissue or organ[[,]] for transplantation into a patient.

Application No.: 09/646,950

Filing Date: December 8, 2000

> 61. (Previously presented) An inhibitor according to Claim 53 wherein the number of amino acid residues in (X_aX_n) is between 2 and 10.

62-68.(Canceled)

69. (Previously presented) A pharmaceutical composition comprising a noncompetitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith, and a pharmaceutically acceptable carrier.

70. (Canceled)

- A method of suppressing or inhibiting the processing of an antigen by an 71. (New) antigen presenting cell, the method comprising contacting the cell with an inhibitor of asparaginyl endopeptidase.
- The method of claim 71, wherein the inhibitor of asparaginyl 72. (New) endopeptidase has the structure Bl-(X_aX_n)Asn-Q wherein B1 is any suitable N terminal blocking group; X_aX_n are the n amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules; Asn is an asparagine residue; and Q is a group capable of reacting with the active site of asparaginyl endopeptidase and forming a covalent complex therewith.
- The method of claim 15, wherein the inhibitor of asparaginyl 73. (New) endopeptidase is said competitive inhibitor.
- (New) The method of claim 71, wherein the method further comprises contacting the cell with an inhibitor of cathepsin S.